

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BEN SACKY Examiner #: 73489 Date: 3/6/02
 Art Unit: 1626 Phone Number 305-6889 Serial Number: 09/909,336
 Mail Box and Bldg/Room Location: CMI 3E11 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods for protection of stratified squamous epithelium etc

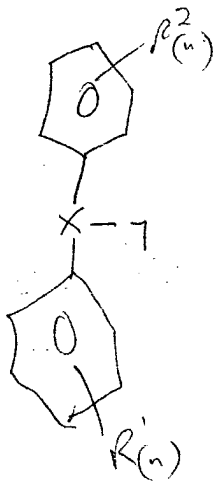
Inventors (please provide full names): Richard Hudson et al.

Earliest Priority Filing Date: 07/07/00

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Methods for protecting stratified squamous epithelium against injury by noxious substances with agents such as

X is a linking group
 Y is OSO_2R^4 etc.

**STAFF USE ONLY**

| | Type of Search | Vendors and cost where applicable |
|--|------------------------|-----------------------------------|
| Searcher: <u>K. Fuller</u> | NA Sequence (#) _____ | STN <u>✓</u> |
| Searcher Phone #: _____ | AA Sequence (#) _____ | Dialog _____ |
| Searcher Location: _____ | Structure (#) <u>1</u> | Questel/Orbit _____ |
| Date Searcher Picked Up: <u>3/7/02</u> | Bibliographic _____ | Dr.Link _____ |
| Date Completed: <u>20</u> | Litigation _____ | Lexis/Nexis _____ |
| Searcher Prep & Review Time: <u>20</u> | Fulltext _____ | Sequence Systems _____ |
| Clerical Prep Time: _____ | Patent Family _____ | WWW/Internet _____ |
| Online Time: <u>34</u> | Other _____ | Other (specify) _____ |

=> FILE REG

FILE 'REGISTRY' ENTERED AT 15:36:56 ON 07 MAR 2002
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STRUCTURE FILE UPDATES: 6 MAR 2002 HIGHEST RN 398994-63-3
DICTIONARY FILE UPDATES: 6 MAR 2002 HIGHEST RN 398994-63-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAPLUS files between
12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved. Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAPLUS files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies. Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=> FILE HCAPLUS

FILE 'HCAPLUS' ENTERED AT 15:37:14 ON 07 MAR 2002
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FILE COVERS 1907 - 7 Mar 2002 VOL 136 ISS 10
FILE LAST UPDATED: 6 Mar 2002 (20020306/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

CAS roles have been modified effective December 16, 2001. Please

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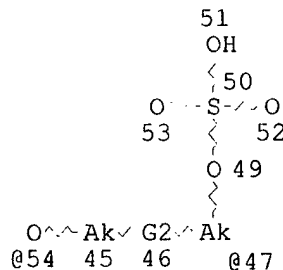
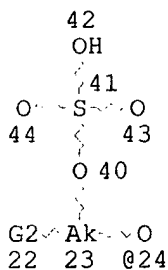
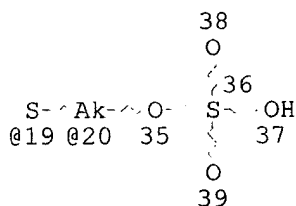
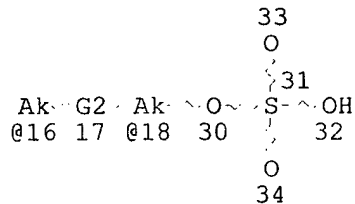
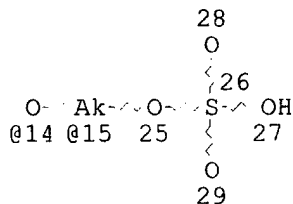
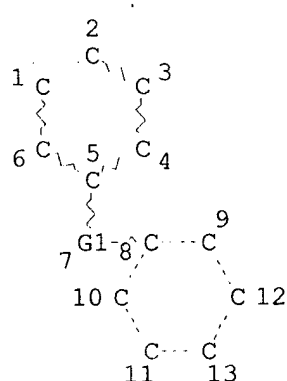
check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> D QUE

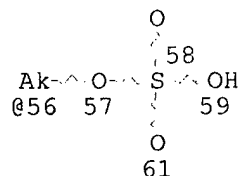
L34

STR



60

Page 1-A



42 structures from this query

Page 2-A

VAR G1=56/19-5 20-8/14-5 15-8/16-5 18-8/21-5 24-8/54-5 47-8

VAR G2=O/S

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

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NUMBER OF NODES IS 59

STEREO ATTRIBUTES: NONE

L36 42 SEA FILE=REGISTRY SSS FUL L34
 L37 22 SEA FILE=HCAPLUS ABB=ON L36 *22 CA references*
 L39 2 SEA FILE=HCAPLUS ABB=ON L37(L)THU/RL
 L40 2 SEA FILE=HCAPLUS ABB=ON L37 AND (SQUAMOUS OR EPITHEL? OR GASTRO?)
 L41 2 SEA FILE=HCAPLUS ABB=ON L39 OR L40
 L43 8 SEA FILE=HCAPLUS ABB=ON L37 AND PHARMAC?/SC,SX
 L44 2 SEA FILE=HCAPLUS ABB=ON L37 AND (ESOPHA? OR HEART? OR GERD OR ?PHARYN?)
 L45 8 SEA FILE=HCAPLUS ABB=ON L41 OR L44 OR L43

8 CA references without utility

=> D L45 ALL 1-8 HITSTR

L45 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:107684 HCAPLUS

DN 136:145195

TI Cadherin-binding assay for identifying compounds which may protect stratified **squamous epithelium** against damage by noxious substances

IN Tobey, Nelia A.; Orlando, Roy C.

PA The Administrators of the Tulane Educational Fund, USA

SO PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-68

CC 1-1 (Pharmacology)

Section cross-reference(s): 6, 13

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| PI WO 2002010767 | A2 | 20020207 | WO 2001-US23717 | 20010726 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI US 2000-626196 | A2 | 20000728 | | |
| AB The invention provides sequences of twenty five proteins and peptide fragments, which have sequence homol. with the extracellular domain of E-cadherin, including desmocollin 3, desmogleins, HA(V/N) domain of group 1 and 2 hemagglutinins from influenza strain A. Novel assay methods for screening compds. or identifying compds. useful for treating gastro-esophageal disease (GERD) are described, which involve detg. the level of or presence of an interaction between the test compd. and a polypeptide sequence comprising a portion of the extracellular domain of the junctional protein E-cadherin or a related polypeptide sequence. ST cadherin binding protein homolog sequence human drug screening; squamous epithelium damage gastroesophageal reflux cadherin binding protein IT Cadherins | | | | |

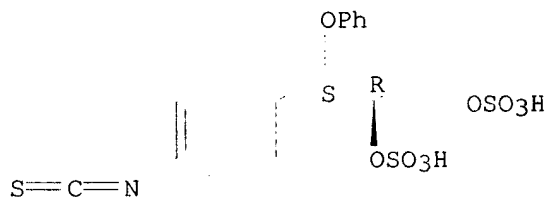
- RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E-; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Gel electrophoresis
(SDS, for det. protein fragmentation; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Plate glass
RL: DEV (Device component use); USES (Uses)
(as solid support for immobilizing cadherin and homologs; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Spheres
(beads, resin, as solid support for immobilizing cadherin and homologs; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Drug screening
Fluorescent indicators
Human
Influenza
Isotope indicators
Poisons, nonbiological source
Protein sequences
Rabbit
(cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Gastric acid
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Hemagglutinins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Cheek
Larynx
Pharynx
(damage, treatment of; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Glycoproteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmocollins, 3; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Glycoproteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological

- study); USES (Uses)
(desmoglein 1; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Glycoproteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmoglein 3; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Glycoproteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmoglein, 2; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Mouth
(**epithelium**, damage, treatment of; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Protein motifs
(extracellular domain; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT HPLC
Mass spectrometry
(for det. protein fragmentation; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Calorimetry
(for det. protein-binding complex stability; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Digestive tract
(**gastroesophageal** reflux, treatment of; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Body fluid
(**gastrointestinal** fluid; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (immobilized, for cadherin-binding assay; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (monoclonal; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Bioassay
(of amino acid, for det. protein fragmentation; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Titration
(of chem. or thermal denaturation, for det. protein-binding complex

- stability; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT **Esophagus**
(permeability; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Biological transport
(permeation, of **esophagus**; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Test tubes
(plastic or glass, as solid support for immobilizing cadherin and homologs; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Plates
(plastic, as solid support for immobilizing cadherin and homologs; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Sulfonic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts or esters; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Glass, uses
Plastics, uses
RL: DEV (Device component use); USES (Uses)
(slide or well, as solid support for immobilizing cadherin and homologs; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT **Epithelium**
(**squamous**, stratified; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Electron density
(tracer; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT Larynx
(vocal cord, damage, treatment of; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 395081-11-5 395081-13-7 395081-15-9 395081-16-0 395081-20-6
395170-80-6 395170-81-7 395170-82-8 395170-83-9 395170-84-0
395170-85-1 395170-86-2 395170-87-3 395170-88-4 395170-89-5
395170-94-2 395170-95-3 395170-96-4 395170-97-5 395170-98-6
395170-99-7 395171-00-3 395171-01-4 395171-02-5 395171-03-6
395171-04-7 395171-05-8
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 9001-37-0, Glucose oxidase 9001-78-9, Alkaline phosphatase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

- (as electron dense tracer; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 616-91-1, N-Acetylcysteine 7647-01-0, Hydrochloric acid, biological studies 9001-75-6, Pepsin
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 51023-76-8P, SITS 57680-56-5P, Sucrose octasulfate 389632-83-1P, CDDD 1192 389632-84-2P, CDDD 1193
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 7664-93-9D, Sulfuric acid, salts or esters
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 9003-99-0, Peroxidase
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (horseradish, as electron dense tracer; cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- IT 389632-83-1P, CDDD 1192 389632-84-2P, CDDD 1193
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (cadherin-binding assay for identifying compds. which may protect stratified **squamous epithelium** against damage by noxious substances)
- RN 389632-83-1 HCAPLUS
- CN 1,2-Propanediol, 3-(4-isothiocyanatophenyl)-3-phenoxy-, bis(hydrogen sulfate) (ester), disodium salt, (2R,3S)- (9CI) (CA INDEX NAME)

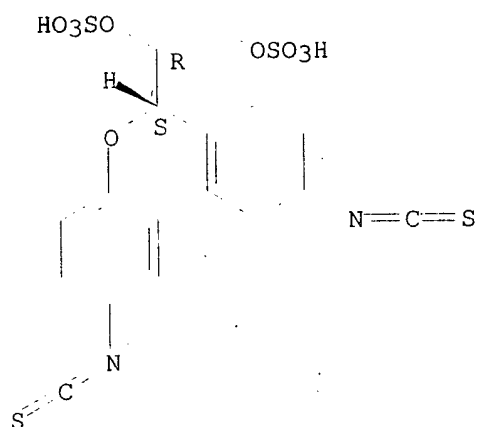
Absolute stereochemistry.



●2 Na

- RN 389632-84-2 HCAPLUS
- CN 1,2-Propanediol, 3-(4-isothiocyanatophenoxy)-3-(4-isothiocyanatophenyl)-, bis(hydrogen sulfate) (ester), disodium salt, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



2 Na

L45 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:51424 HCAPLUS

DN 136:102181

TI Preparation of sulfate ester agents for protection of stratified
squamous epithelium against injury by noxious substances

IN Hudson, Richard A.; Tobey, Neila A.; Orlando, Roy C.; Tillekeratne,
Liyanaaratchinge M. V.

PA The Administrators of the Tulane Educational Fund, USA; University of
Toledo

SO PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DT Patent

LA English

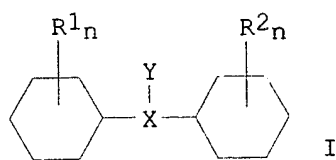
IC ICM C07C305-18

ICS C07C331-28; A61K031-255

CC 25-13 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2002004411 | A1 | 20020117 | WO 2001-US21328 | 20010705 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| PRAI | US 2000-216771 | P | 20000707 | | |
| OS | MARPAT 136:102181 | | | | |
| GI | | | | | |



AB Sulfate ester agents I [X = OCH₂, CH₂O; Y comprises at least one OSO₃R₄ moiety, wherein R₄ is H or a pharmaceutically acceptable cation; n = 1-3; R₁, R₂ = H, halogen with an at. no. from 9 to 53, SO₃R₄, NCS, NCO, NH(CO)OR₃, NH(CS)SR₃, NH(C:NH)OR₃, NHCOCH₂Cl, NHCOCH₂Br, NHCOCH:CH₂, etc.], agents for treating **gastroesophageal** reflux disease, were prepd. E.g., a mixt. of phenol, NaOH, and water was treated with styrene oxide to give 2-phenoxy-2-phenylethanol. The product was dissolved in dry pyridine and was treated with pyridine-sulfur trioxide to give 2-phenoxy-2-phenylethanesulfate sodium salt.

ST sulfate ester agent prepn **gastroesophageal** reflux disease

IT Digestive tract

(**gastroesophageal** reflux; prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT Larynx

(laryngitis; prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT Pharynx

(**pharyngitis**; prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT Digestive tract

(pyrosis; prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT 389118-86-9P 389632-71-7P, CDDD 1185

389632-74-0P, CDDD 1187 389632-77-3P, CDDD 1188

389632-81-9P, CDDD 1189 389632-82-0P, CDDD 1190

389632-83-1P, CDDD 1192 389632-84-2P, CDDD 1193

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT 96-09-3, Styrene oxide 103-90-2, 4-Acetamidophenol 106-48-9,

4-Chlorophenol 108-95-2, Phenol, reactions 555-16-8,

4-Nitrobenzaldehyde, reactions 2051-66-3 98819-68-2,

(2R,3R)-3-Phenylglycidol

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

IT 1885-07-0P 35271-56-8P 49678-08-2P, trans-4-Nitrocinnamaldehyde

53574-80-4P, 2-Phenoxy-2-phenylethanol 389118-87-0P,

(2R,3S)-3-Phenoxy-3-phenylpropane-1,2-diol 389118-88-1P 389118-89-2P

389118-90-5P 389118-91-6P 389118-92-7P 389118-93-8P

389118-94-9P 389118-95-0P 389118-96-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(prepn. of sulfate ester agents as agents for treating **gastroesophageal** reflux disease)

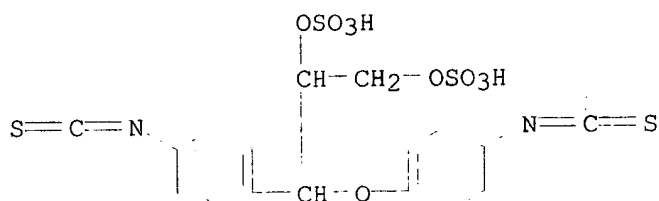
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

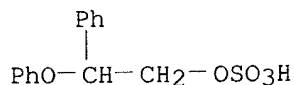
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 IT 389118-86-9P 389632-71-7P, CDDD 1185
 389632-74-0P, CDDD 1187 389632-77-3P, CDDD 1188
 389632-81-9P, CDDD 1189 389632-82-0P, CDDD 1190
 389632-83-1P, CDDD 1192 389632-84-2P, CDDD 1193
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (prepn. of sulfate ester agents as agents for treating
 gastroesophageal reflux disease)
 RN 389118-86-9 HCAPLUS
 CN 1,2-Propanediol, 3-(4-isothiocyanatophenoxy)-3-(4-isothiocyanatophenyl)-,
 bis(hydrogen sulfate) (ester) (9CI) (CA INDEX NAME)



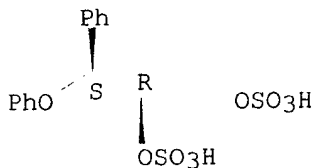
RN 389632-71-7 HCAPLUS
 CN Benzeneethanol, .beta.-phenoxy-, hydrogen sulfate, sodium salt (9CI) (CA
 INDEX NAME)



● Na

RN 389632-74-0 HCAPLUS
 CN 1,2-Propanediol, 3-phenoxy-3-phenyl-, bis(hydrogen sulfate), disodium
 salt, (2R,3S)- (9CI) (CA INDEX NAME)

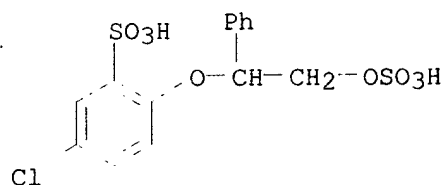
Absolute stereochemistry.



2 Na

RN 389632-77-3 HCAPLUS

CN Benzenesulfonic acid, 5-chloro-2-[1-phenyl-2-(sulfooxy)ethoxy]-, disodium salt (9CI) (CA INDEX NAME)

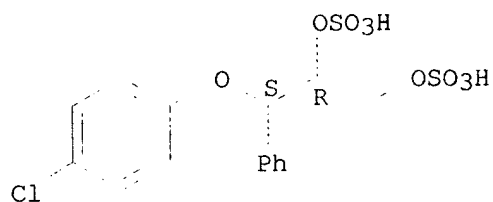


● 2 Na

RN 389632-81-9 HCAPLUS

CN 1,2-Propanediol, 3-(4-chlorophenoxy)-3-phenyl-, bis(hydrogen sulfate), disodium salt, (2R,3S)- (9CI) (CA INDEX NAME)

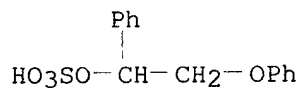
Absolute stereochemistry.



● 2 Na

RN 389632-82-0 HCAPLUS

CN Benzenemethanol, .alpha.-(phenoxymethyl)-, hydrogen sulfate, sodium salt (9CI) (CA INDEX NAME)

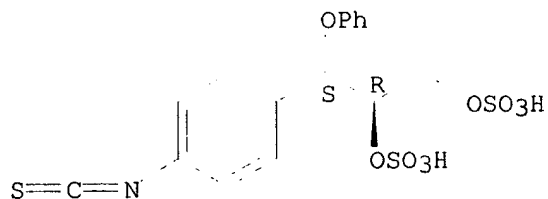


● Na

RN 389632-83-1 HCAPLUS

CN 1,2-Propanediol, 3-(4-isothiocyanatophenyl)-3-phenoxy-, bis(hydrogen sulfate) (ester), disodium salt, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

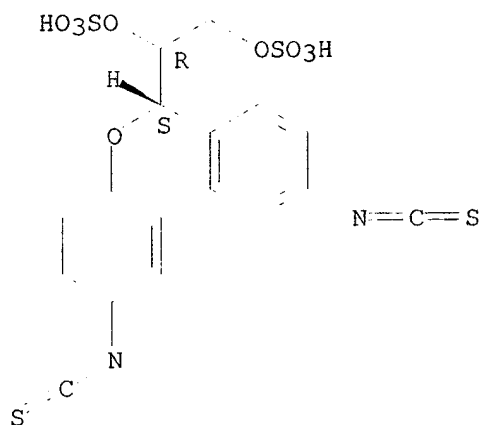


● 2 Na

RN 389632-84-2 HCAPLUS

CN 1,2-Propanediol, 3-(4-isothiocyanatophenoxy)-3-(4-isothiocyanatophenyl)-, bis(hydrogen sulfate) (ester), disodium salt, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 Na

IT 389118-91-6P 389118-92-7P 389118-94-9P

389118-95-0P 389118-96-1P

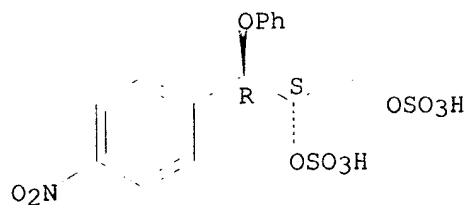
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of sulfate ester agents as agents for treating gastroesophageal reflux disease)

RN 389118-91-6 HCAPLUS

CN 1,2-Propanediol, 3-(4-nitrophenyl)-3-phenoxy-, bis(hydrogen sulfate) (ester), disodium salt, (2S,3R)- (9CI) (CA INDEX NAME)

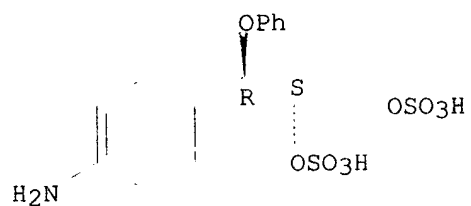
Absolute stereochemistry.



●2 Na

RN 389118-92-7 HCAPLUS
 CN 1,2-Propanediol, 3-(4-aminophenyl)-3-phenoxy-, bis(hydrogen sulfate)
 (ester), disodium salt, (2S,3R)- (9CI) (CA INDEX NAME)

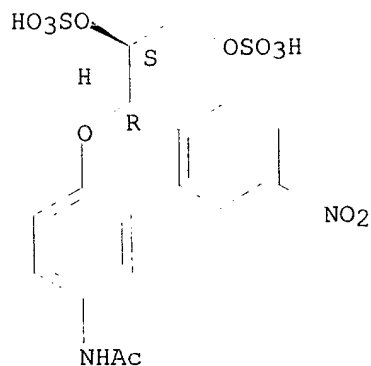
Absolute stereochemistry.



●2 Na

RN 389118-94-9 HCAPLUS
 CN 1,2-Propanediol, 3-[4-(acetylamino)phenoxy]-3-(4-nitrophenyl)-,
 bis(hydrogen sulfate) (ester), disodium salt, (2S,3R)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

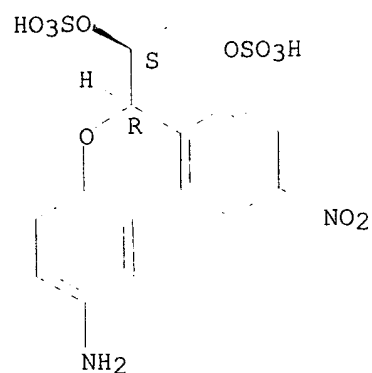


●2 Na

RN 389118-95-0 HCAPLUS

CN 1,2-Propanediol, 3-(4-aminophenoxy)-3-(4-nitrophenyl)-, bis(hydrogen sulfate) (ester), disodium salt, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

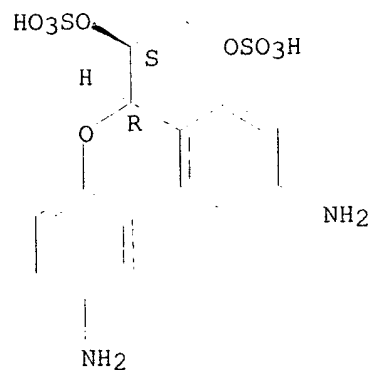


2 Na

RN 389118-96-1 HCAPLUS

CN 1,2-Propanediol, 3-(4-aminophenoxy)-3-(4-aminophenyl)-, bis(hydrogen sulfate) (ester), disodium salt, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



2 Na

L45 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:136010 HCAPLUS

DN 132:303094

TI Characterization of the Major DNA Adduct Formed by .alpha.-Hydroxy-N-desmethyldamoxifen in Vitro and in Vivo

AU Gamboa da Costa, Goncalo; Hamilton, L. Patrice; Beland, Frederick A.; Marques, M. Matilde

CS Centro de Quimica Estrutural Complexo I, Instituto Superior Tecnico, Lisbon, 1049-001, Port.

SO Chem. Res. Toxicol. (2000), 13(3), 200-207

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CODEN: CRTOEC; ISSN: 0893-228X

PB American Chemical Society

DT Journal

LA English

CC 1-6 (Pharmacology)

AB Tamoxifen is hepatocarcinogenic in rats and has been assocd. with an increased risk of endometrial cancer in women. Recent reports suggest that it may be genotoxic in humans. N-desmethyltamoxifen is a major tamoxifen metabolite that has been proposed to be responsible for one of the major adducts detected in liver DNA of rats treated with tamoxifen. The metabolic activation of N-desmethyltamoxifen to DNA binding products may involve oxidn. to .alpha.-hydroxy-N-desmethyltamoxifen followed by esterification. In the study presented here, the authors report the synthesis of .alpha.-hydroxy-N-desmethyltamoxifen and the characterization of the major adduct obtained from .alpha.-sulfoxy-N-desmethyltamoxifen in vitro as (E)-.alpha.-(deoxyguanosin-N2-yl)-N-desmethyltamoxifen. In addn., the authors use 32P-postlabeling in combination with HPLC to compare the adducts formed in the livers of female Sprague-Dawley rats treated by gavage with tamoxifen or equimolar doses of .alpha.-hydroxy-N-desmethyltamoxifen. The authors conclude that one of the major adducts formed in vivo and previously suggested to derive from N-desmethyltamoxifen is chromatog. identical to .alpha.-(deoxyguanosin-N2-yl)-N-desmethyltamoxifen.

ST hydroxydesmethyltamoxifen DNA adduct formation; tamoxifen metabolite DNA adduct formation

IT DNA

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 10540-29-1, Tamoxifen 265321-60-6

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 162070-61-3P

RL: BPR (Biological process); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 223762-19-4

RL: FMU (Formation, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 185993-92-4 265321-61-7

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 19076-79-0

RL: RCT (Reactant)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

IT 265321-58-2P 265321-59-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(characterization of major DNA adduct formed by tamoxifen metabolite hydroxydesmethyltamoxifen in vitro and in vivo)

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD

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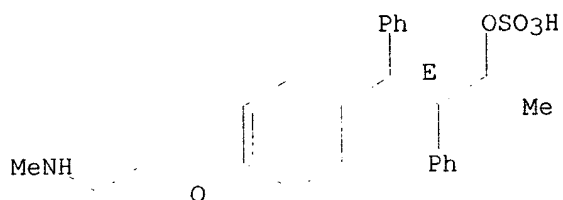
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 IT 265321-60-6
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (characterization of major DNA adduct formed by tamoxifen metabolite
 hydroxydesmethyldtamoxifen in vitro and in vivo)
 RN 265321-60-6 HCAPLUS
 CN Benzeneethanol, .alpha.-methyl-.beta.-[[4-[2-(methylamino)ethoxy]phenyl]ph
 enylmethylene]-, hydrogen sulfate (ester), (.beta.E)- (9CI) (CA INDEX
 NAME)

Double bond geometry as shown.



L45 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:814067 HCAPLUS
 DN 130:148214
 TI Lifetime and Reactivity of an Ultimate Tamoxifen Carcinogen: The Tamoxifen
 Carbocation
 AU Sanchez, Cristina; Shibutani, Shinya; Dasaradhi, Lakkaraju; Bolton, Judy
 L.; Fan, Peter W.; McClelland, Robert A.
 CS Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
 SO J. Am. Chem. Soc. (1998), 120(51), 13513-13514
 CODEN: JACSAT; ISSN: 0002-7863
 PB American Chemical Society
 DT Journal
 LA English
 CC 1-2 (Pharmacology)
 Section cross-reference(s): 22, 26
 AB The aq. lifetime and deoxyguanosine reactivity of the carbocation obtained
 by metab. of tamoxifen is directly detd. The cation has been implicated
 as the source of DNA binding obsd. with this drug, and the results add
 considerable support to this model.
 ST tamoxifen carbocation lifetime reactivity carcinogen
 IT Solvolysis
 Solvolysis kinetics
 (lifetime and reactivity of a tamoxifen carbocation metabolite as a
 carcinogen)
 IT 10540-29-1, Tamoxifen
 RL: BPR (Biological process); RCT (Reactant); THU (Therapeutic use); BIOL
 (Biological study); PROC (Process); USES (Uses)
 (lifetime and reactivity of a tamoxifen carbocation metabolite as a
 carcinogen)
 IT 220257-97-6P 220257-99-8P 220258-01-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (lifetime and reactivity of a tamoxifen carbocation metabolite as a
 carcinogen)
 IT 961-07-9, Deoxyguanosine
 RL: RCT (Reactant)

(reaction with tamoxifen carbocation; lifetime and reactivity of a tamoxifen carbocation metabolite as a carcinogen)

IT 185993-88-8P 185993-89-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solvolysis of; lifetime and reactivity of a tamoxifen carbocation metabolite as a carcinogen)

IT 97151-02-5P 97170-41-7P

RL: MFM (Metabolic formation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(sulfation of; lifetime and reactivity of a tamoxifen carbocation metabolite as a carcinogen)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 185993-88-8P 185993-89-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solvolysis of; lifetime and reactivity of a tamoxifen carbocation metabolite as a carcinogen)

RN 185993-88-8 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.E)- (9CI) (CA INDEX NAME)

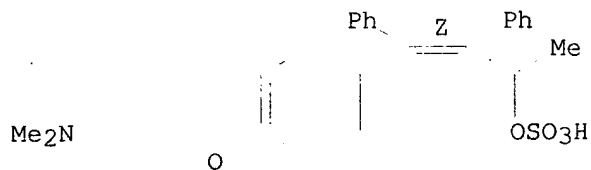
Double bond geometry as shown.



RN 185993-89-9 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L45 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:345680 HCAPLUS

DN 129:90045

TI The metabolic activation of tamoxifen and .alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes proceeds via sulfation

AU Davis, Warren; Venitt, Stan; Phillips, David H.

CS Section of Molecular Carcinogenesis, Institute of Cancer Research, Haddow Laboratories, Sutton, Surrey, SM2 5NG, UK

SO Carcinogenesis (1998), 19(5), 861-866

CODEN: CRNGDP; ISSN: 0143-3334

PB Oxford University Press

DT Journal

LA English

CC 1-6 (Pharmacology)

AB The biotransformation pathway of tamoxifen and .alpha.-hydroxytamoxifen to DNA-binding species was investigated in rat hepatocytes in vitro. Rat hepatocytes were isolated by in situ collagenase perfusion and then maintained in sulfate-free Dulbecco's modified Eagle's medium. Magnesium sulfate was added to the medium to give concns. of 0-10 .mu.M, prior to treatment for 18 h with solvent vehicle (DMSO), tamoxifen (10 .mu.M), .alpha.-hydroxytamoxifen (1 .mu.M) or benzo[a]pyrene (BaP) (10 and 50 .mu.M). DNA was isolated and analyzed by 32P-post-labeling. For tamoxifen and .alpha.-hydroxytamoxifen, the level of DNA adduct formation was directly proportional to the concn. of sulfate in the medium. Between 0 and 10 .mu.M MgSO4, the DNA adduct level increased 10-fold with both compds. Rat hepatocytes were also maintained in normal Dulbecco's modified Eagle's medium and pretreated with dehydroisoandrosterone-3-sulfate (DHEAS, a sulfotransferase inhibitor) at concns. ranging from 0-1 mM, prior to treatment with solvent vehicle (DMSO), tamoxifen (10 .mu.M), .alpha.-hydroxytamoxifen (1 .mu.M) or BaP (50 .mu.M). For tamoxifen and .alpha.-hydroxytamoxifen the level of DNA adducts was reduced to approx. one-fifth by the addn. of DHEAS (0.1 .mu.M). BaP-DNA adduct formation,

which proceeds by a pathway that does not require sulphation, was not significantly affected by sulfate concn. or by addn. of DHEAS, which demonstrates that the general metabolic capacity and viability of the hepatocytes were not compromised. It is concluded that the activation of tamoxifen in rat liver cells to DNA binding products proceeds predominantly through hydroxylation followed by sulfate ester formation at the .alpha.-position of the Et side chain.

ST tamoxifen sulfation DNA binding genotoxicity carcinogen

IT DNA

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(binding to; metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

IT Carcinogens

Genotoxicity

Hepatocyte

Hydroxylation (biological)

Sulfation (biological)

(metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

IT 10540-29-1, Tamoxifen

RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES
(Uses)

(metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

IT 52228-01-0, Hydroxy steroid sulfotransferase

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

(metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

IT 97151-02-5, .alpha.-Hydroxytamoxifen 185993-88-8

RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)

(metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

IT 185993-88-8

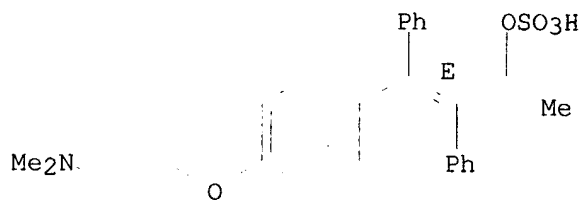
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological
study); FORM (Formation, nonpreparative); PROC (Process)

(metabolic activation via sulfation of tamoxifen and
.alpha.-hydroxytamoxifen to DNA-binding species in rat hepatocytes in
carcinogenicity study)

RN 185993-88-8 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene
]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.E)- (9CI) (CA INDEX
NAME)

Double bond geometry as shown.



- L45 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
 AN 1997:476356 HCAPLUS
 DN 127:185307
 TI Oxo substituents markedly alter the phase II metabolism of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen
 AU Ramakrishna, Kornepati V.; Fan, Peter W.; Boyer, C. Scott; Dalvie, Deepak; Bolton, Judy L.
 CS Department of Medicinal Chemistry and Pharmacognosy (M/C 781) College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612-7231, USA
 SO Chem. Res. Toxicol. (1997), 10(8), 887-894
 CODEN: CRTOEC; ISSN: 0893-228X
 PB American Chemical Society
 DT Journal
 LA English
 CC 1-2 (Pharmacology)
 AB The P 450-catalyzed hydroxylation of tamoxifen to give .alpha.-hydroxytamoxifen [(E)-4-{4-[2-(dimethylamino)ethoxy]phenyl}-3,4-diphenyl-3-buten-2-ol] and subsequent formation of reactive sulfate esters which alkylate DNA has been proposed to be a potential carcinogenic pathway for tamoxifen. In the present study, the ability of .alpha.-hydroxytamoxifen analogs to form GSH and sulfate conjugates was investigated in order to understand the structural features influencing reactivity. The para oxo analogs 1 [1-(4-methoxyphenyl)-3-hydroxy-1-butene], 2 [1-(4-hydroxyphenyl)-3-hydroxy-1-butene], and 4 [1-(4-hydroxyphenyl)-1-phenyl-3-hydroxy-1-butene] reacted with GSH instantaneously under strong acidic conditions to yield GSH conjugates in greater than 90% yields. Interestingly, the meta phenolic analogs 3 [1-(3-hydroxyphenyl)-3-hydroxy-1-butene] and 5 [1-(3-hydroxyphenyl)-1-phenyl-3-hydroxy-1-butene] did not react with GSH to any significant extent under similar conditions. Characterization of the GSH conjugates with 1H-NMR, electrospray mass spectrometry, and UV showed that all of the conjugates resulted from attack of GSH at the .alpha.-position of the substrates with displacement of the hydroxyl group. The formation of a single pair of diastereomeric conjugates strongly supported adduct formation to proceed through a direct SN2 displacement mechanism and not through a quinone methide (4-alkyl-2,5-cyclohexadien-1-one) intermediate. At physiol. pH and temp. only the para hydroxy analogs 2 and 4 gave GSH conjugates, a reaction which seems to be catalyzed by isoforms of glutathione S-transferase. Similar substituent effects were obsd. in the sulfotransferase-mediated formation of .alpha.-hydroxy sulfate esters in that only the para hydroxy analogs formed conjugates at the aliph. hydroxyl group. Finally, the present investigation showed a remarkable difference in the reactivities of para and meta phenolic analogs of .alpha.-hydroxybutenylbenzenes toward GSH and sulfate conjugation reactions.
 ST hydroxylation tamoxifen phase II metab carcinogen; hydroxybutenylbenzene tamoxifen biotransformation model
 IT Carcinogens

- Drug metabolism
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT DNA adducts
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT Hydroxylation
(.alpha.-; oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT Structure-activity relationship
(.alpha.-hydroxylation-modifying; oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 10540-29-1, Tamoxifen
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 173612-08-3
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 70-18-8, GSH, biological studies 9023-09-0, Sulfotransferase 9035-51-2, Cytochrome P 450, biological studies 50812-37-8, Glutathione S-transferase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 68047-06-3, 4-Hydroxytamoxifen 97151-02-5 185993-88-8 194279-77-1
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 10540-29-1DP, Tamoxifen, analogs 97151-02-5DP, analogs
RL: BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)
- IT 77254-94-5DP, glutathione conjugates 120727-58-4P 134747-45-8P 194279-78-2DP, derivs 194279-78-2DP, glutathione conjugates 194279-78-2P 194279-79-3DP, derivs 194279-79-3P 194279-80-6P 194279-81-7P 194279-82-8P 194279-83-9P 194279-84-0P 194279-85-1P 194279-86-2P 194279-87-3DP, glutathione conjugates 194279-88-4DP, derivs 194279-88-4DP, glutathione conjugates 194279-89-5DP, glutathione conjugates 194279-90-8DP, glutathione conjugates 194279-91-9DP, glutathione conjugates 194279-92-0P 194279-93-1P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)

IT 100-83-4, 3-Hydroxybenzaldehyde 123-08-0, 4-Hydroxybenzaldehyde
 13020-57-0, 3-Hydroxybenzophenone
 RL: RCT (Reactant)
 (oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)

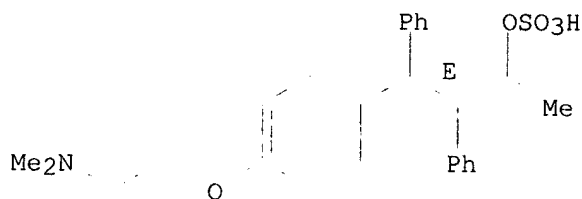
IT 3160-35-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)

IT 185993-88-8
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (oxo substituents effects on phase II metab. of .alpha.-hydroxybutenylbenzenes: models probing the bioactivation mechanisms of tamoxifen)

RN 185993-88-8 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L45 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
 AN 1997:113040 HCAPLUS
 DN 126:98923
 TI Identification of Tamoxifen-DNA Adducts Formed by .alpha.-Sulfate Tamoxifen and .alpha.-Acetoxytamoxifen
 AU Dasaradhi, Lakkaraju; Shibutani, Shinya
 CS Department of Pharmacological Sciences, State University of New York, Stony Brook, NY, 11794-8651, USA
 SO Chem. Res. Toxicol. (1997), 10(2), 189-196
 CODEN: CRTOEC; ISSN: 0893-228X
 PB American Chemical Society
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 AB .alpha.-Sulfate trans-tamoxifen and .alpha.-sulfate cis-tamoxifen were synthesized as proposed active metabolites of tamoxifen that react with DNA. .alpha.-Acetoxytamoxifen was prepd. as a model-activated form to produce a reactive carbocation. -Calf thymus DNA was reacted with .alpha.-hydroxytamoxifen or the activated forms of tamoxifen, and tamoxifen-DNA adducts were analyzed by a 32P-postlabeling method. The reactivity of .alpha.-sulfate trans-tamoxifen to DNA was much higher than that of .alpha.-hydroxytamoxifen. The formation of tamoxifen-DNA adducts

induced by .alpha.-acetoxytamoxifen and .alpha.-sulfate cis-tamoxifen was 1100- and 1600-fold, resp., higher than that of .alpha.-hydroxytamoxifen. Both .alpha.-sulfate tamoxifens and .alpha.-acetoxytamoxifen were highly reactive to 2'-deoxyguanosine. Four reaction products of dG-tamoxifen were isolated by HPLC and characterized by mass- and proton magnetic resonance spectroscopy. Fractions 1 and 2 that eluted first were identified as the epimers of trans form of dG-N2-tamoxifen. Fractions 3 and 4 were identified as the epimers of cis form of dG-N2-tamoxifen. When DNA was reacted with .alpha.-acetoxytamoxifen in vitro, three isomers of dG-N2-tamoxifen were detected: fraction 2 was the major adduct while fractions 1 and 3 were minor adducts.

ST tamoxifen metabolite prepn DNA adduct isolation; acetoxytamoxifen DNA adduct prepn isolation; antitumor tamoxifen metabolite prepn DNA adduct; sulfate tamoxifen DNA adduct prepn isolation

IT DNA

RL: BSU (Biological study, unclassified); BIOL (Biological study) (identification of tamoxifen-DNA adducts formed by .alpha.-sulfate tamoxifen and .alpha.-acetoxytamoxifen)

IT 185993-88-8P 185993-89-9P 185993-90-2P

185993-91-3P 185993-92-4P 185993-93-5P

RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(identification of tamoxifen-DNA adducts formed by .alpha.-sulfate tamoxifen and .alpha.-acetoxytamoxifen)

IT 185993-88-8P 185993-89-9P 185993-90-2P

185993-91-3P

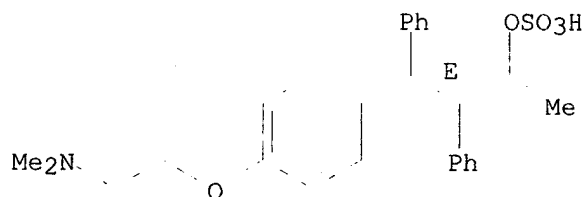
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(identification of tamoxifen-DNA adducts formed by .alpha.-sulfate tamoxifen and .alpha.-acetoxytamoxifen)

RN 185993-88-8 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.E)- (9CI) (CA INDEX NAME)

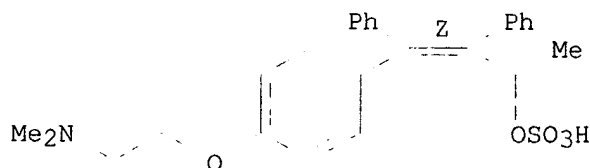
Double bond geometry as shown.



RN 185993-89-9 HCAPLUS

CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (.beta.Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

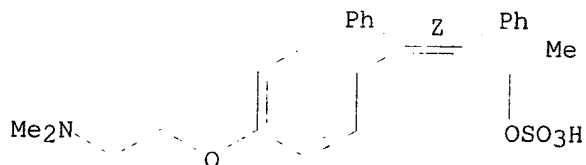


RN 185993-90-2 HCAPLUS
CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (Z)-, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

CM 1

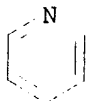
CRN 185993-89-9
CMF C26 H29 N O5 S

Double bond geometry as shown.



CM 2

CRN 110-86-1
CMF C5 H5 N



RN 185993-91-3 HCAPLUS
CN Benzeneethanol, .beta.-[[4-[2-(dimethylamino)ethoxy]phenyl]phenylmethylene]-.alpha.-methyl-, hydrogen sulfate (ester), (E)-, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 185993-88-8
CMF C26 H29 N O5 S

Double bond geometry as shown.



CM 2

CRN 110-86-1
CMF C5 H5 N



L45 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1971:74581 HCAPLUS
DN 74:74581
TI Metabolism of orphenadrine citrate in man
AU Ellison, Theodore; Snyder, Albert; Bolger, James W.; Okun, Ronald
CS Riker Lab., Northridge, Calif., USA
SO J. Pharmacol. Exp. Ther. (1971), 176(2), 284-95
CODEN: JPETAB
DT Journal
LA English
CC 15 (Pharmacodynamics)
GI For diagram(s), see printed CA Issue.
AB After receiving oral doses of orphenadrine citrate (I citrate), 4
healthymen excreted the following metabolites in their urine:
N-monodemethylorphenadrine, N,N-didemethylorphenadrine, orphenadrine
N-oxide, and the glucuronide (sulfate) conjugates of o-
methylbenzhydroxyacetic acid and o-methylbenzhydrol. Minor amts. of free
o-methylbenzhydrol and o-methylbenzhydroxyacetic acid were also excreted.
ST orphenadrine metab men; diphenhydramines metab
IT 4682-36-4
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of)
IT 5472-13-9 10488-36-5 20263-93-8 29215-00-7 32190-19-5
32205-92-8 32720-22-2 32720-23-3
RL: BIOL (Biological study)
(of urine, as orphenadrine metabolite)
IT 32190-19-5
RL: BIOL (Biological study)
(of urine, as orphenadrine metabolite)
RN 32190-19-5 HCAPLUS
CN Benzhydrol, 2-methyl-, hydrogen sulfate (8CI) (CA INDEX NAME)

